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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,377	04/12/2004	Robert D. Groneberg	03-086-A	4839

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EXAMINER
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SEAMAN, D MARGARET M

ART UNIT	PAPER NUMBER
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1625

MAIL DATE	DELIVERY MODE
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06/04/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/823,377	Applicant(s) GRONEBERG ET AL.	
	Examiner /D. Margaret Seaman/	Art Unit 1625	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 March 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-62 is/are pending in the application.
- 4a) Of the above claim(s) 1-13 and 28-61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14-27 & 62 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of group XI in the reply filed on 2/7/2007 is acknowledged. The traversal is on the ground(s) that the search for groups I, XIII and XV are coextensive with the search of group XI. This is not found persuasive because the compounds have different formulas and different definitions. Due to this it is unclear as to exactly how these different formulas are related to each other.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-13 and 28-61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/6/07.

3. This application contains claims drawn to an invention nonelected with traverse in the reply filed on 3/6/07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 14-27 and 62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of formula II' wherein C is cyclohexyl or cyclopentyl substituted in the 1 position with R', the phenyl ring of the C bicycle has only one substituent in the 6 position (when C is a cyclohexyl) or 5 position (when C is cyclopentyl) wherein the substituent is -alkyl-amine, the amine can be either N-di(Alkyl), NH(alkyl) or piperidine; Ra is H; R1 is phenyl and R2 is naphthyl, does not reasonably provide enablement for where C is a 4 or 7-membered carbocyclic ring or any heterocyclic ring; R1 heteroaryl or any aryl other than phenyl; R2 is morpholine or quinoline, i.e. heterocyclic or arylalkenyl or other aryl other than naphthalene; Ra is alkyl or aryl; R3, R4 and R5 are halo, CN CF3 or other of the moieties listed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in

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the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims,
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

**The nature of the invention:** The nature of the invention is the compounds that are useful for treating a disorder that is modulated by the bradykinin receptor.

**The state of the prior art:** The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

**The predictability in the art:** It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable

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an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects of all diseases, whether or not the modulation of bradykinin receptors would make a difference in the disease. Hence, in the absence of a showing of a nexus between any and all known diseases and the modulation of bradykinin receptors, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 due to the unpredictability of the role of modulation of bradykinin receptors.

**The presence or absence of working examples:** The only examples of the instant formula II' that have been made and tested for bradykinin activity are wherein C is either 5- or 6- membered carbocyclic ring substituted in the 1 position with R', the phenyl ring of the C bicycle has only one substituent in the 6 position (when C is a cyclohexyl) or 5 position (when C is cyclopentyl) wherein the substituent is -alkyl-amine, the amine can be either N-di(Alkyl), NH(alkyl) or piperidine; Ra is H; R1 is phenyl and R2 is naphthyl.

**The amount of direction or guidance present:** The guidance present in the specification is the entirety of the markush claimed will work to modulate bradykinin. However the only part that has been taught is the part that is described above.

**The breadth of the claims:** The claims are drawn to the entirety markush of the formula II' and its utility to treat conditions mediated by bradykinin.

**The quantity of experimentation needed:** The quantity of experimentation needed is undue. One skilled in the art would need to determine what direction to proceed to find compounds that able to modulate bradykinin out of the large markush of the instant claims.

**The level of the skill in the art:** The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of claim 1 for the treatment of any disease. As a result necessitating one of ordinary skill to perform an exhaustive search for which diseases can be treated by which compound of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would

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have to engage in undue experimentation to test which compounds could be used to modulate bradykinin, with no assurance of success.

This rejection can be overcome by amending the claims to be commensurate in scope with the enable subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to /D. Margaret Seaman/ whose telephone number is 571-272-0694. The examiner can normally be reached on 730am-4pm, Monday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/D. Margaret Seaman/  
Primary Examiner  
Art Unit 1625

dms